

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2006/003974

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K47/10 A61K47/12 A61K31/565 A61P5/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, FSTA, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2003/022877 A1 (DUDLEY ROBERT E) 30 January 2003 (2003-01-30) cited in the application page 1, paragraph 3 page 8, paragraph 61 page 17; example 4 claims 1-7, 11, 12 page 9, paragraph 69 -----	1-17
Y	MÜLLER ET AL.: "Testosterontherapie des Hypogonadismus" SCHWEIZERISCHE ÄRZTEZEITUNG, vol. 81, no. 46, 2000, pages 2589-2593, XP002389108 page 2591, paragraph 2 page 2591, paragraph 5 ----- -/-	1-17

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

Date of the actual completion of the international search

28 July 2006

Date of mailing of the international search report

04/09/2006

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2006/003974

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SHAPIRO J ET AL: "TESTOSTERONE AND OTHER ANABOLIC STEROIDS AS CARDIOVASCULAR DRUGS" AMERICAN JOURNAL OF THERAPEUTICS, CHAPMAN AND HALL, NEW YORK, NY, US, vol. 6, no. 3, May 1999 (1999-05), pages 167-174, XP009004530 ISSN: 1075-2765 page 829, paragraph 4 page 832, paragraph 2 -----	1-17
Y	SIMON ET AL.: "Androgen Therapy Improves Insulin Sensivity and Decreases Leptin Level in Healthy Adult Men With Low Plasma Total Testosterone" DIABETES CARE, vol. 24, no. 12, December 2001 (2001-12), pages 2149-2151, XP002389109 page 2149, column 2, paragraph 2 page 2151, column 2 -----	1-17
Y	US 6 503 894 B1 (DUDLEY ROBERT E ET AL) 7 January 2003 (2003-01-07) cited in the application claims 1,2,5-9 -----	1-17
A	"Long-Term Testosterone Gel (AndroGel) Treatment Maintains Beneficial Effects on Sexual Function and Mood, Lean, and Fat Mass, and Bone Mineral Density in Hypogonadal Men" J. CLIN. ENDOCRINOL. METAB., vol. 85, no. 5, May 2004 (2004-05), pages 2085-2098, XP002389110 page 2085, paragraph 1 page 2086, paragraph 3 page 2095, column 2 -----	1-17

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2006/003974

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003022877	A1	30-01-2003	NONE
US 6503894	B1	07-01-2003	AU 9059801 A 13-03-2002
			BR 0113670 A 09-11-2004
			CN 1527714 A 08-09-2004
			EP 1313482 A1 28-05-2003
			HU 0302921 A2 28-01-2004
			MA 27127 A1 03-01-2005
			NO 20030961 A 25-04-2003
			PL 366117 A1 24-01-2005
			WO 0217926 A1 07-03-2002
			US 2003050292 A1 13-03-2003
			US 2002183296 A1 05-12-2002
			US 2003232072 A1 18-12-2003
			ZA 200301686 A 19-04-2004
			ZA 200301687 A 13-09-2004
			ZA 200301705 A 08-07-2004

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2006/003974

International filing date (day/month/year)
07.04.2006

Priority date (day/month/year)
08.04.2005

International Patent Classification (IPC) or both national classification and IPC
INV. A61K47/10 A61K47/12 A61K31/565 A61P5/50

Applicant
LABORATOIRES BESINS INTERNATIONAL

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Date of completion of
this opinion

see form
PCT/ISA/210

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2006/003974

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2006/003974

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-17
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-17
Industrial applicability (IA)	Yes: Claims	1-17
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item III.

The term "steroid in the testosterone synthetic pathway" is unclear and moreover relates to an extremely large number of possible substances. It is not obvious which steroids result from the testosterone synthetic pathway. This would require an equally unquantifiable and thus unreasonable amount of experimentation, imposing a severe and undue burden on all those wishing to ascertain the scope of the claim, which is not in compliance with the clarity requirement of Article 6 PCT. The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search (PCT Guidelines, 9.19 and 9.24).

The extent of the search was consequently limited to the clearly defined active ingredients disclosed in the application, in fact to

androisoxazole, androstenedione, bolasterone, clostebol, ethylestrenol, formyldienolone, 4-hydroxy-19-nortestosterone, methenolone, methyltrienolone, nandrolone, oxymesterone, quinbolone, stenbolone, trenbolone, boldenone, dehydroepiandrosterone, fluoxymesterone, mestanolone, mesterolone, methandrostenolone, 17-alpha-methyltestosterone, 17-alpha-methyl-testosterone 3-cyclopentyl enoether, norethandrolone, normethandrone, oxandrolone, oxymetholone, prasterone, stanbolone, stanozolol, dihydrotestosterone, testosterone, anagestone, chlormadinone acetate, delmadinone acetate, demegestone, dimethisterone, dihydrogesterone, ethinylestrenol, ethisterone, ethynodiol, ethynodiol diacetate, flurogestone acetate, gestodene, gestonorone caproate, haloprogesterone, 17-hydroxy-16-methylene-progesterone, 17-alpha-hydroxyprogesterone, 17-alpha-hydroxyprogesterone caproate, medrogestone, medroxyprogesterone, megestrol acetate, melengestrol, norethindrone, norethindrone acetate, norethynodrel, norgesterone, norgestimate, norgestrel, norgestrienone, 19-norprogesterone, norvinisterone, pentagestrone, prenenolone, progesterone, promegestone, quingestron, and trengestron

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Documents

Reference is made to the following documents

- D1: US 2003/022877 A1 (DUDLEY ROBERT E) 30 January 2003 (2003-01-30)
cited in the application
- D2: MÜLLER ET AL.: "Testosterontherapie des Hypogonadismus"
SCHWEIZERISCHE ÄRZTEZEITUNG, vol. 81, no. 46, 2000, pages 2589-2593,
XP002389108

2. Independent Claim 1

- 2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of **claim 1** does not involve an inventive step in the sense of Article 33(3) PCT.
- 2.2 The document D1 is regarded as being the closest prior art to the subject-matter of claim 1 and discloses a composition comprising 0.1 - 10% testosterone, 30 - 98% alcohol selected from the group consisting of ethanol and isopropanol, 0.1 - 5% isopropylmyristate, 1 - 5% sodium hydroxide, and 0.1 - 5% of a gelling agent (claim 1). The hydroalcoholic gel is applied for the treatment of testosterone deficient disorders such as hypogonadism, sexual dysfunction, hyperglycemia, hyperinsulinemia, hypoinsulinemia which are listed on p. 8, paragraph 81.
- 2.3 The subject-matter of **claim 1** therefore differs from this known in that the composition is applied for the treatment and/or prevention of diabetes.
- 2.4 The problem to be solved by the present invention may therefore be regarded as providing a formulation for the treatment of diabetes.
- 2.5 The solution proposed in **claim 1** of the present application cannot be considered as involving an inventive step (Article 33(3) PCT), because D1 already discloses the composition of the claimed hydroalcoholic gel and mentions that hyperglycemia and

hypoinsulinemia are among the diseases which are treated by application of the testosterone comprising gel. This already indicates that the gel might be used for the treatment of diabetes. D2 discloses that the application of testosterone increases the insulin sensitivity, so that testosterone application is recommended for the treatment of diabetes typ -2. Furthermore, the document indicates that diabetes mellitus is often associated with a testosterone deficiency and provides a link to D1. Therefore, it would have been obvious for the person skilled in the art to combine the teachings of the two documents. Moreover, the application does not give any evidence that diabetes can be treated with testosterone, it merely describes the implementation of a clinical trial without providing results. Therefore, the problem is not solved and the subject-matter of claim 1 does not involve an inventive step.

- 2.6 Dependent **claims 2 - 17** do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, because the subject-matter of these claims is already disclosed in D1.

3. INDUSTRIAL APPLICABILITY (Art. 33(4) PCT)

- 3.1 The subject-matter of **claims 1 - 17** is industrial applicable according to Art. 33(4) PCT.